REMARKS

Claims 1, 4, 5, 7-10, 13, 14, 16-19, 21-25, 27, 28, and 30-34 are presently pending. Claims 31-34 are new; Applicants submit that claims 32-33 belongs in the same restriction group as the claims currently under consideration, and so request consideration thereof. Claims 1-9, 25, 27, 28, and 30 were withdrawn by the Examiner after restriction, and claims 2-3, 6, 11-12, 15, 20, 26, and 29 have been cancelled, leaving claims 10, 13, 14, 16-19, 21-24 and 32 under consideration. Claims 1, 4, 5, 8-10, 13, 14, 16-19, 21-25, 27, 28, and 30 are amended by the present submission. Support for these amendments can be found throughout the application as filed, including, e.g., page 4, lines 3-8; page 4, line 30 – page 5, line 15; page 13, line 2; page 16, lines 4-11; page 24, line 16 – page 25, line 8; and the claims as filed. Support for new claims 31-34 can be found throughout the application as filed, including, e.g., page 30, line 9 – page 32, line 6. No new matter has been added.

Objection to Declaration

The Examiner objected to the declaration for lacking citizenship information for the inventor. A new declaration is submitted herewith.

Rejection under 35 USC §112, ¶2

The Examiner rejected claims 13 and 18 as allegedly indefinite for being dependent on non-elected claim 12. Claim 13 has been cancelled, and amended claim 18 depends from elected claim 10. Applicants therefore request withdrawal of the rejection under 35 USC §112, ¶2.

Rejection under 35 USC §102(b)

Claims 10, 13, 16 and 17 were rejected as allegedly anticipated by Ramiya et al., J. Autoimmun. 9(3):349-56 (1996). As noted above, claim 13 has been cancelled, rendering the rejection thereto moot. Claim 10 as amended is drawn to compositions comprising human preproinsulin or an immunologically active fragment or variant thereof, and a Montanide ISA adjuvant or an equivalent thereof. Ramiya et al. discloses the use of IFA, but does not disclose the use of Montanide ISA adjuvants. Montanide ISA adjuvants differ from IFA at least in that they are purer than standard IFA; the Montanide ISA adjuvants undergo more rigorous quality control procedures to obtain greater purity and thus cause less unwanted side effects such as

inflammation (see, e.g., the application as filed, page 24, line 2 – page 25, line 8). In particular, Montanide ISA adjuvants differ from IFA at least as a result of the use of a refined mannide oleate surfactant, e.g., Montanide 80. Further, IFA is not recommended for use in humans as recognized by Ramiya et al., who used alum.

Applicants submit that the claims as amended are not anticipated by the Ramiya et al. reference, and request withdrawal of the rejection under 35 USC § 102(b).

Rejections under 35 USC § 103(a)

Claim 18 was rejected as allegedly obvious over Ramiya et al. in view of U.S. Pat. No. 6,462,185 (the '185 patent). Claim 18 depends from claim 10, and thus incorporates all of the limitations contained therein. As noted above, Ramiya et al. does not disclose the use of Montanide ISA adjuvants. The '185 patent does not supply the disclosure that is lacking in Ramiya, i.e., it has no disclosure relating to either insulin or Montanide ISA adjuvants, let alone the combination of the two. The '185 patent is about flower organ specific promoters, and fails to even provide any general teachings about the use of urea to solubilize proteins. Applicants submit that the claims as amended are not obvious over the Ramiya et al. reference in view of the '185 patent, and request withdrawal of the rejection under 35 USC § 103(a).

Claims 19, 21, 23, and 24 were rejected as allegedly obvious over Ramiya et al. in view of U.S. Pat. No. 4,281,061 (the '061 patent). Claim 23 has been cancelled, rendering moot the rejection thereto. As noted above, Ramiya et al. does not disclose the use of Montanide ISA adjuvants. The '061 patent does not supply the disclosure that Ramiya et al. lacks, and the portion cited by the Examiner merely notes that reagents for use in an immunoassay can conveniently be provided in kits. Applicants submit that the claims as amended are not obvious over the Ramiya et al. reference in view of the '061 patent, and request withdrawal of the rejection under 35 USC § 103(a).

Claim 22 was rejected as allegedly obvious over Ramiya et al. in view of the '061 patent and further in view of U.S. Pat. No. 5,447, 843 (the '843 patent). As noted above, Ramiya et al. does not disclose the use of Montanide ISA adjuvants. Also as discussed above, the '061 patent does not supply the disclosure that Ramiya et al. lacks, nor does the '843 patent supply the

disclosure that is lacking in Ramiya. The '843 patent merely discloses that heat shock proteins in a kit can be lyophilized. Again, there is no disclosure relating to insulin, Montanide ISA adjuvants, or the combination thereof. Applicants submit that the claims as amended are not obvious over the Ramiya et al. reference in view of the '061 patent and/or the '843 patent, and request withdrawal of the rejection under 35 USC § 103(a).

Rejection under 35 USC §112, ¶1

Claims 13, 18, 19, and 21-24 were rejected as allegedly lacking written description support for the term "an immunologically active fragment or variant." As noted above, claim 13 has been cancelled, rendering the rejection thereto moot. Applicants respectfully traverse.

As a first matter, the specification teaches that preproinsulin has the sequence of SEQ ID NO:1. see, e.g., page 15, lines 20-30. Further, the specification teaches that insulin B chain includes amino acids 25-54 of SEQ ID NO:1; the B chain is an "immunologically active fragment or variant" of the human preproinsulin; see, e.g., page 4, lines 3-5; and page 16, lines 8-11. Preproinsulin is only 110 amino acids, and the B chain is a total of only 30 amino acids, thus the number of variants is limited. Methods for making and testing other fragments and variants that are immunologically active are conventional in the art; furthermore, as the Examiner noted, a number of methods for making and testing the claimed fragments and variants are disclosed in the application.

In this case, the species disclosed (e.g., the 30 amino acid B chain and the fragment comprising residues 33-47 of SEQ ID NO:1) are sufficient to describe the entire genus, which is limited both functionally (the fragments and variants must be immunogenic) and quantitatively (the relatively small size of preproinsulin); see, e.g., "Example 14: Protein by Function" of the Revised Written Description Guidelines – Training Materials, available at uspto.gov/web/patents/guides.htm.

Applicants submit that the pending claims satisfy the written description requirement and request withdrawal of the rejection under 35 USC § 112, ¶1.

For at least the foregoing reasons, Applicants submit that the claims as amended are patentable, and request rapid notification of the same.

Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 8/1/05

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